**REMARKS**

Claims 1, 2, 6 and 10 presently appear in this case. No claims have been allowed. The official action of August 23, 2006, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention is directed to methods for treating conditions wherein TNF is to be eliminated from the body or its effect in the body is to be antagonized by administering the TNF-binding protein of the present invention.

The examiner has objected to the specification as failing to provide proper antecedent basis for the claimed subject matter. The examiner notes that the amended claim language of "said protein being of sufficient purity to allow determination of the N-terminal amino acid sequence thereof" does not appear in the specification. The examiner has indicated that correction of the specification to add such antecedent basis would not constitute new matter, as the specification teaches protein purification (page 19) and the N-terminal amino acid sequencing of said protein (pages 25-26).

The present specification has now been amended at the bottom of page 25 in order to state:

> This sequence analysis establishes that the TNF Inhibitory Protein of the invention was of sufficient purity to allow determination of the N-terminal amino acid sequence thereof.

This sentence establishes antecedent basis for the claim language and does not constitute new matter because, as the examiner has acknowledged, the specification teaches protein purification on page 19 and the N-terminal amino acid sequencing of that said protein at pages 25-26. Accordingly, this amendment obviates the objection to the specification. Reconsideration and withdrawal thereof is therefore respectfully urged.

Claims 1, 2, 6 and 10 have been rejected under 35 U.S.C. 103(a), as being unpatentable over Seckinger et al. (1988), in view of Dayer. The examiner acknowledges applicant's argument that the new claim limitation of sufficient purity to allow N-terminal sequencing is sufficient to define over the prior art. However, the examiner states that such argument is not sufficient to overcome the prior art rejection because there is no evidence indicating that what had been accomplished in the instant application, i.e., partial N-terminal sequencing of the polypeptide, could not have been achieved by using Seckinger's purified inhibitor of TNF-α. The examiner concludes that the purity limitation therefore is not sufficient to distinguish the presently

claimed polypeptide from that of Seckinger. This rejection is respectfully traversed.

In order to provide evidence that partial N-terminal sequencing of the polypeptide as accomplished by the present specification could not have been achieved by using Seckinger's purified inhibitor of TNF-α, attached is a declaration of Dr. Rik Derynck. Dr. Derynck has been responsible for running a research lab since 1981 and for the last twenty-five years has combined molecular biology, cell biology, and protein biochemistry in his approaches to scientific questions. He has hands-on experience with protein purification and has provided guidance to others working in his lab on protein purification projects.

As can be seen by his declaration, Dr. Derynck has analyzed the disclosure of the Seckinger et al. (1988) publication and several other publications of about the same period relating to the purification of the same protein inhibitor of TNF-α. He first points out that the Seckinger et al. (1988) publication itself recognizes at page 1515 that they were not in possession of a purified protein. The publication itself recognizes that many bands are still being identified in SDS-PAGE and that the nature of the protein remains to be determined by purification to homogeneity.

Dr. Derynck explains how purification of a protein found in a biological fluid is a challenging and complex matter and that in order to derive sequence information directly from one such protein, the protein of interest needs to be purified to an extent that it is the predominant protein in the preparation that will be subjected to the sequencing method. In his analysis of the literature, he notes that another two years went by following Seckinger et al. (1988) before that laboratory was able to purify the protein sufficiently to allow N-terminal sequencing. Furthermore, two other groups were seeking to isolate and sequence the same protein. All of these groups required much more stringent purification than was described by Seckinger et al. (1988).

As stated on page 15 of his declaration, Dr. Derynck points out that, in contrast to the later publications of the Seckinger group, Seckinger et al. (1988) did not provide any evidence for purification, nor was the generation of purified protein claimed by the authors. Instead, this paper reports two purification experiments, i.e., a fractionation of the urinary protein mixture using Sephacryl S200, and a fractionation by Mono P chromatofocusing. Dr. Derynck points out that each of these experiments presents a single fractionation step; no disclosure of the sequential use of these two methods was even presented. Dr. Derynck then

explains, with reference to the literature, why these single steps illustrate only a very low degree of purification. Dr. Derynck's analysis establishes that the admittedly impure active fractions of Seckinger et al. (1988) correspond to at least twenty percent of the protein, suggesting a 5-fold enrichment, while subsequent papers establish that a 54,000-81,000 fold purification is required to have protein of sufficient purity for sequencing.

In the paragraph bridging pages 16 and 17 of his declaration, Dr. Derynck states:

> Thus, I can opine with a very high degree of certainty, based on the above described evidence, that the product of the Seckinger et al (1988) publication was insufficiently pure to allow sequencing using the technology available *circa* 1990.

The evidence presented herein to support the fact that the impure composition of Seckinger et al. (1988) could not have allowed N-terminal sequencing is in the form of the professional opinion of an independent expert in the field, which is supported by the objective evidence appearing in the literature references analyzed. Accordingly, there is now sufficient evidence of record for the examiner to accept the fact that the material of Seckinger et al. (1988) is insufficiently pure to permit N-terminal sequencing. Therefore, it does not anticipate the material used in the process of the present invention and, accordingly, no

combination of Seckinger and Dayer can render obvious the processes of the present invention that require the use of a TNF-binding protein of sufficient purity to allow determination of the N-terminal amino acid sequence thereof. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. 112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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